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Comparison of subjective and objective measures of constipation– employing a new method for categorizing gastrointestinal symptoms

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Abstract

Introduction: Correlations between subjective and objective measures of constipation have seldom been demonstrated. This could be due to multiple confounding factors in clinical studies and the broad span of symptoms represented in questionnaires used to assess constipation. We developed a new method for categorizing gastrointestinal (GI) symptoms into relevant symptom groups, and used this in a controlled experimental study aimed to investigate whether GI transit times and colonic volumes were correlated to self-reported GI symptoms.

Methods: Twenty-five healthy male participants were enrolled in a randomized, double-blinded, placebo-controlled, five-day crossover study with the treatments oxycodone and placebo. Objective measures of GI transit times and colonic volumes were obtained by the means of the 3D-Transit System and magnetic resonance colonography, whereas subjective GI symptoms were measures via three validated questionnaires. The symptoms were then categorized into five groups; "abdominal symptoms", "defecation difficulties", "incomplete bowel evacuation", "reduced bowel movement frequency", and "stool symptoms". Spearman's rank order correlation was used to determine correlations between the five groups of symptoms and the objective measures.

Results: No correlations between the GI symptoms and transit times or colonic volumes were found (all $P > 0.05$).

Discussion: GI transit times and colonic volumes were not correlated to self-reported GI symptoms even in a controlled experimental study and when symptoms were categorized into relevant symptom groups. Thus, both subjective and objective measures must be considered relevant when assessing constipation in clinical and research settings, ensuring that both physiological aspects as well as the severity and impact of symptoms experienced by patients can be assessed.

Keywords: Gastrointestinal, Methods, Opioids, Questionnaires, Transit time, Colonic volume

Introduction

Constipation is a common condition that affects people of all ages, with a prevalence estimation of up to 27 percent in the population of Western countries (Pare, Ferrazzi, Thompson, Irvine, & Rance, 2001; Peppas, Alexiou, Mourtzoukou, & Falagas, 2008). The causes of constipation are multiple, ranging from physical inactivity, pharmacological-induced motility dysfunction (e.g. induced by opioids and anticholinergics), to advanced cancer illness (Hayat, Dugum, & Garg, 2017). To handle constipation in the clinic, and to investigate physiological mechanisms of constipation in research studies, valid subjective and objective methods are of great importance. Subjective questionnaires such as the Bowel Function Index (BFI) and Cleveland Clinical Constipation scores are commonly used to evaluate the severity and impact of gastrointestinal (GI) symptoms experienced by patients with constipation, and to guide clinicians in diagnostics and choice of treatment (Argoff et al., 2015). The purpose of objective measures is to gain insights into underlying physiological aspects of GI function, and to assess the efficacy of pharmacological treatment options (Matias Nilsson et al., 2016; Olesen & Drewes, 2011). Usually, a combination of measures are applied. However, if subjective and objective measures of constipation are directly correlated, it may be beneficial utilizing merely the subjective measures as this would reduce clinical trial costs, ease participant discomforts, and increase compliance (Grønlund et al., 2018; Stotzer, Fjälling, Grétarsdóttir, & Abrahamsson, 1999). Nevertheless, previous clinical studies regarding GI function in patients with constipation have not found any correlations between subjective and objective measures (Chaussade et al., 1989; Cowlam et al., 2008; Knudsen, Krogh, Østergaard, & Borghammer, 2017). An explanation for this may lie within the design of clinical studies in which confounding factors, e.g. multiple GI diseases, psychological factors, and concomitant drug use to a great extent can

influence the results. A better alternative may be to investigate such correlations in a more controlled setting, e.g. in opioid-induced constipation in healthy participants. Opioids cause GI dysmotility through multiple mechanism; decreased neuronal excitability of the enteric nervous system, decreased gut secretion and gut sphincter dysfunction (Brock et al., 2012). Thus, Nilsson et al., and Poulsen et al., recently conducted a crossover study employing a model of oxycodone-induced constipation to investigate whether self-reported GI symptoms (measured with three questionnaires) were correlated to GI transit times (measured with the 3D-Transit system), and colonic volumes (measured using magnetic resonance imaging (MRI)) (Matias Nilsson et al., 2016; Poulsen et al., 2016).

However, no correlations between the subjective and objective measures were found here either. This could be due to the very broad span of symptoms appearing in the applied questionnaires.

Thus, it may be beneficial to stratify the GI symptoms assessed in the questionnaires and categorize these into relevant symptoms groups, to simplify the correlations and decrease the risk of type 1 errors. The aim of the current study was to investigate correlations between GI symptoms and GI transit time/colonic volume using a new method categorizing symptoms into symptom-and GI regions-specific groups approach. We hypothesized that using this approach, significant correlations between the subjective and objective measures would be found.

Methods

Data source

The study from which these data origin was designed as a randomized, double-blinded, placebo-controlled, crossover trial to assess how opioids affect the GI tract. The North Denmark Region Committee on Health Research Ethics (N-20130030) and the Danish Medicines Agency (2013070299) approved the study, and it was conducted in accordance with the principles of ICH-GCP of the European Union. The full trial protocol is registered at www.clinicaltrialsregister.eu (EudraCT no. 2013-001540-60). Twenty-five healthy male participants with no current symptoms or history of GI disease were recruited. All underwent a screening session in which a physician obtained their medical history and performed a physical examination, and the participants gave written informed consent. The study consisted of two separate five-day periods, in which the participants were randomized using computer generated block-randomization to receive either oral prolonged-release oxycodone (OxyContin®, 5 mg twice on day 1, 10 mg twice on day 2-4, and 10 mg once on day 5) or placebo. Medication was provided by Mundipharma Research Ltd (Cambridge, UK). In short, oxycodone treatment induced constipation by the means of significantly increased GI symptoms, increased total GI transit time and colonic transit time, and increased volume in the cecum/ascending- and transverse colon. Further details on in- and exclusion criteria, study design, experimental procedures, and results are found in the previous publications from the study (Matias Nilsson et al., 2016; Poulsen et al., 2016). For the current sub-study, merely data from the oxycodone treatment period was used in the correlation analyses.

Subjective measures

To assess GI symptoms, participants filled in the Danish versions of three well-validated questionnaires; The BFI (Table 1), the Gastrointestinal Symptom Rating Scale (GSRS) (Table 2),

and the Patient Assessment of Constipation Symptoms (PAC-SYM) (Table 3). The BFI and GSRS were filled in at day 1 and 5, whilst PAC-SYM was filled in once daily throughout the study period. For the present study, data from day 5 of all three questionnaires were used in the correlation analyses.

The BFI is a 3-item questionnaire to measure constipation. All three items are evaluated by the patient on a numeric analogue scale from 0 to 100 where 0 = no problems and 100 = most severe problems. The BFI has been validated against bowel movements and laxative use, and assesses the severities of three GI symptoms; defecation difficulties, feeling of incomplete evacuation, and personal judgement of constipation (Ducrotté & Caussé, 2012; Rentz, Yu, Müller-Lissner, & Leyendecker, 2009). The symptoms are rated on a numerical rating scale from 0-10, 0 signifying 'not at all' and 10 signifying 'very strong'. It is the only scale specially designed for opioid-induced constipation (Olesen & Drewes, 2011).

Table 1. The Bowel Function Index (BFI) items.

ITEM
1. Ease of defecation during the last 7 days according to patient assessment
2. Feeling of incomplete bowel evacuation during the last 7 days according to patient assessment
3. Personal judgment of patient regarding constipation during the last 7 days

The GSRS is a well-validated questionnaire composing of 15 items assigned to five syndromes: gastroesophageal reflux, abdominal pain, indigestion, diarrhoea, and constipation. Each question is rated on a 7-point Likert scale, where 1 represents absence of symptoms and 7 represents very

bothersome symptoms (Kulich et al., 2008; Revicki, Wood, Wiklund, & Crawley, 1998). The subjects

used the Danish version of the GSRS including an appendix of six questions related to dryness of the mouth, nausea, anorexia, dysphagia, need to push and squeeze when trying to pass a stool or during defecation.

Table 2. The Gastrointestinal Symptom Rating Scale (GSRS) syndromes and items.

SYNDROME	**ITEM**	
Gastroesophageal reflux	2.	Heartburn
	3.	Acid regurgitation
Abdominal pain	1.	Abdominal pains
	4.	Sucking sensation in the epigastrium
	5.	Nausea and vomiting
Indigestion	6.	Borborygmus
	7.	Abdominal distension
	8.	Eructation
	9.	Increased flatus
Diarrhea	11.	Increased passage og stools
	12.	Loose stools
	14.	Urgent need for defecation
Constipation	10.	Decreased passage of stools
	13.	Hard stools
	15.	Feeling of incomplete evacuation

The PAC-SYM has been validated with a high test-retest reliability, and is a 12-item questionnaire assigned to three domains: abdominal symptoms, rectal symptoms, and stool symptoms (Frank, Kleinman, Farup, Taylor, & Miner, 1999; Slappendel, Simpson, Dubois, & Keininger, 2006). Each question is rated on a 5-point Likert scale, where 0 represents absence of symptoms and 4 represents very severe symptoms. Responses are scored as 0=absence of symptom, 1=mild, 2=moderate, 3=severe and 4=very severe.

Table 3. Patient Assessment of Constipation Symptoms (PAC-SYM) domains and items.

DOMAIN	**ITEM**
Abdominal	1. Discomfort in your stomach
	2. Pain in your stomach
	3. Bloating in your stomach
	4. Stomach cramps
Rectal	5. Painful bowel movements
	6. Rectal burning during or after bowel movement
	7. Rectal bleeding or tearing during or after bowel movement
Stool	8. Incomplete bowel movements, like you did not finish
	9. Bowel movements that were to hard
	10. Bowel movements that were to small
	11. Straining or squeezing to try to pass a bowel movement
	12. Feeling like you had to pass a bowel movement but could not (“false alarm”)

Symptom categorization

To categorize symptoms into relevant groups, homogenization of the questionnaires was necessary. Thus, the GSRS scale was modified from 1-7 to 0-6 in order to have a “true zero” corresponding the

BFI and PAC-SYM. Hereafter, all three questionnaires were converted into 0-100 scales. This modification assumed that the level between each number were equal between all questionnaires, and that the minimum and maximum levels were equal. Collectively, the questionnaires included 36 questions, each referring to a specific GI symptom. The number of times the participants reported a specific symptom (i.e. a score ≥ 1) were counted, as done in a previous study (Amanzio, Corazzini, Vase, & Benedetti, 2009). A symptom was included in the correlation analyses if the following three criteria were met: 1) ≥ 15 % of the participants reported the specific symptom on day 5 (Burns et al., 1999; Nakamura, Osonoi, & Terauchi, 2010), 2) the number of participants reporting the specific symptom increased with ≥ 15 % from day 1 to day 5, and 3) the symptom was related to either the small intestine, colon or anal sphincter, as these were the areas of the GI tract assessed with the objective measures. This selection resulted in a total of 18 symptoms, which were categorized into the following five groups; "abdominal symptoms", "defecation difficulties", "incomplete bowel evacuation", "reduced bowel movement frequency", and "stool symptoms" based on their physiological relations (Amanzio, Benedetti, & Vase, 2012; Amanzio et al., 2009). The procedure for categorizing the symptoms into groups is illustrated in Figure 1. To obtain a total score for each group, mean composite scores were calculated and baseline-corrected, resulting in scores for each group in the range of -100 to 100.

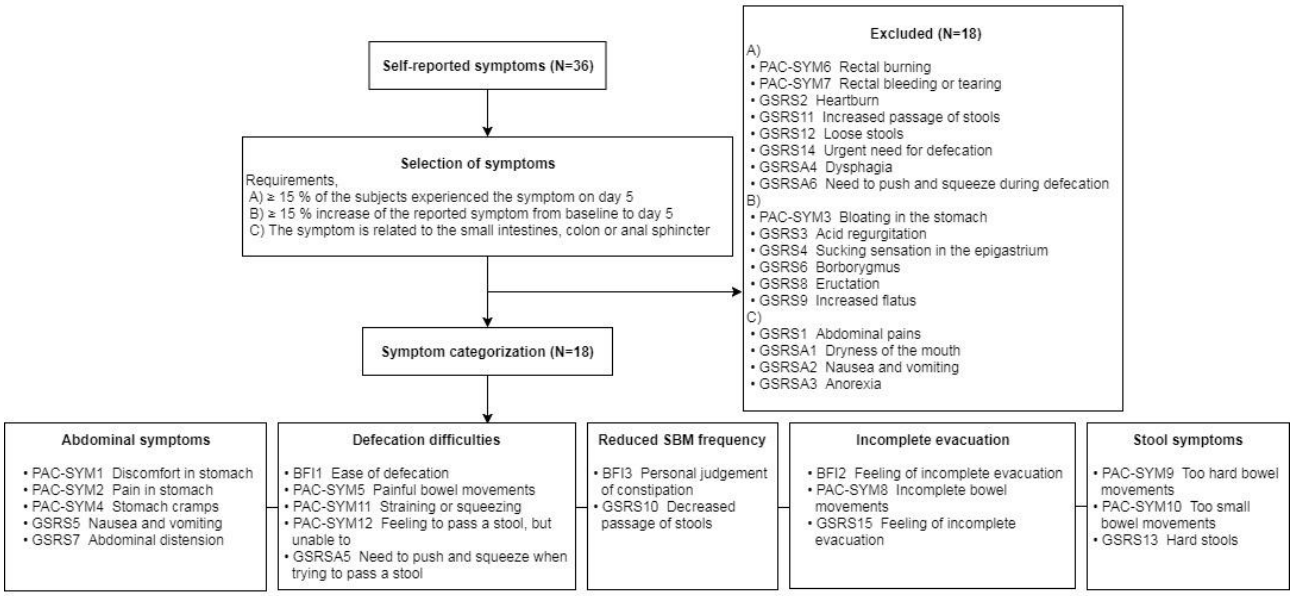

Figure 1. Categorization of the self-reported GI symptoms. The numbers indicated next to questionnaire abbreviations represent the order of the questions in each of the questionnaires. For example, the PAC-SYM6 refers to the sixth question in the PAC-SYM questionnaire. BFI: The bowel function index, GSRS: The gastrointestinal symptom rating scale, GSRSA: The gastrointestinal symptom rating scale appendix question. PAC-SYM: The patient assessment of constipation symptoms.

Objective measures

Gastrointestinal transit time

On day 1, after administration of the first study medication dose, participants had a standardized meal, and the 3D-Transit capsule was swallowed with a glass of water. Participants were instructed to carry a detector fitted to the abdomen in an elastic belt, in order to track the 3D-Transit capsule throughout the GI tract.

The 3D-Transit system is a novel, well-validated, minimally invasive tool for the ambulatory evaluation of total and segmental GI transit times (Haase et al., 2014; Kalsi et al., 2018). Technical

specifications of the system, and detailed information on data analysis, is described in details elsewhere (Haase et al., 2014; Poulsen et al., 2016). In short, total GI - and regional (small intestine and colon) transit times were determined manually by a trained researcher using specialized software (Motilis Medica SA, Lausanne, Switzerland). Changes in contraction frequencies observed on capsule rotation graphs and 2D plots of the anatomical position were used to determine when the capsule progressed from the stomach into the duodenum, i.e. gastric emptying (a shift in contraction frequency from 3 to 9-12 contractions per minute) and from the ileum to the right colon (from 9-12 to 3 contractions per minute). The total GI transit time was defined as the time between ingestion and expulsion of the capsule. If the capsule had not been expelled by day 5, the time of the last confirmed capsule-signal was used as the earliest possible expulsion time. Segmental colonic transit times (ascending/cecum, transverse, descending and rectosigmoid) were determined using a custom MATLAB (R2015b version 8.6, MathWorks, Inc, Natick, MA, USA) application, allowing the researcher to determine the capsule passage from the hepatic flexure, splenic flexure and the descending-sigmoid junction (Figure 2A), a method previously validated (Poulsen et al., 2016).

Figure 2. Objective measurement methods. (A) 3D-Transit recording of capsule transit through the colon. Blue dots indicate capsule progression according, where each hour of recording is written in numbers. Colorectal segments are chosen according to landmarks (hepatic flexure, splenic flexure, and the end of descending colon) shown by red arrows. (B) MRI of the abdomen. Regions of interest surround colonic segments; yellow is ascending colon, red is transverse colon, green is descending colon, and blue is rectosigmoid colon.

Colonic volume

All MRI scans were acquired using a GE Discovery MR450 1.5 T MRI System (GE Healthcare, Milwaukee, Wisconsin, USA). Participants were scanned in a fasting state in the morning of days 1 and 5 to assess the amount of faces in colon, however, only colonic volume on day 5 (baseline-corrected) were used for the present correlation analyses. Total and segmental colonic volumes were determined using semiautomatic in-house data analysis software, which has previously been validated (Sandberg et al., 2015). In short, colonic content was manually outlined on each of the 40 MRI slices encapsulating the following colonic segments; ascending colon, transverse colon, descending colon, and rectosigmoid colon (Figure 2B). Hereafter, the software automatically determined the exact boundaries of the colon and calculated the fecal volume of each colonic region. Detailed description of the specific settings for the MRI scans and calculations of colonic volumes are described elsewhere (M. Nilsson et al., 2015; Sandberg et al., 2015).

Statistics

Spearman's rank-order correlations was used to determine correlations between the five side symptom groups and the objective measures (total GI - and regional transit times, total and segmental colonic volumes). A Spearman's Rho of ±0.00 to ±0.30 was considered a negligible correlation, ±0.30 to ±0.50 a low correlation, ±0.50 to 0.70 a moderate correlation, ±0.70 to ±0.90 a high correlation, and ±0.90 to ±1.00 a very high correlation (Mukaka, 2012). Analyses were carried out using SPSS (Version 25.0, IBM Corp., New York, USA), and due to multiple comparisons, *P*-values of < 0.01 were considered statistically significant. All data are reported as medians [IQR], unless otherwise stated.

Results

All participants filled in the three questionnaires on day 5. Recordings of total GI - and regional transit time were obtained in all participants (25 recordings in total), however, it was not possible to determine segmental colonic transit times in 2/25 recordings, due to insufficient data quality. MRI scans were missed in 6/25 cases because of capsule retention on day 5 (excluding MRI assessment), thus 19 measures of total and segmental colonic volumes were available for the present analyses.

The median total GI transit time was 43.9 hours [7.1 - 92.6 hours]. The median total colonic volume was 881 mL [783 - 979 mL]. Median scores of the five symptom groups are presented in Table 4.

No correlations between the symptom groups against total GI - or regional transit times and total or segmental colonic volumes were found (all $P > 0.1$; all $|r| < 0.4$) (Table 4).

Table 4. Correlations between the symptom groups and the objective measures; transit time and colonic volume after 5-days of oxycodone treatment in healthy males. Spearman's correlation coefficient (r): ±0.00 to ±0.30; a negligible correlation, ±0.30 to ±0.50: a low correlation, ±0.50 to 0.70; a moderate correlation, ±0.70 to ±0.90; a high correlation, ±0.90 to ±1.00; a very high correlation. SBM: Spontaneous bowel movement; r: Spearman's correlation coefficient.

	Abdominal symptoms	**Defecation difficulties**	**Reduced SBM frequency**	**Incomplete evacuation**	**Stool symptoms**
Questionnaire score on	9.6 ± 16.5	31.5 ±	39.2 ±	26.6 ±	26.6 ±

day 5		30.0	27.8	28.0	28.7
Transit time					
Small intestine, r | P-value	0.04 | 0.85	-0.01 | 0.97	0.09 | 0.67	-0.17 | 0.45	0.02 | 0.92
All colon, r | P-value	0.05 | 0.81	-0.01 | 0.98	0.08 | 0.74	-0.16 | 0.47	-0.30 | 0.18
Ascending colon, r | P-value	-0.10 | 0.65	-0.25 | 0.25	-0.16 | 0.46	-0.10 | 0.69	-0.33 | 0.13
Transverse colon, r | P-value	0.20 | 0.37	0.22 | 0.32	0.12 | 0.60	-0.24 | 0.27	-0.02 | 0.92
Descending colon, r | P-value	0.06 | 0.79	-0.01 | 0.97	0.24 | 0.28	-0.12 | 0.57	-0.26 | 0.23
Rectosigmoid colon, r | P-value	0.15 | 0.51	0.12 | 0.60	-0.19 | 0.38	-0.19 | 0.38	-0.03 | 0.90
Total GI tract, r | P-value	0.07 | 0.75	0.03 | 0.90	0.08 | 0.70	-0.19 | 0.37	-0.29 | 0.17
Colonic volume					
All colon, r | P-value	0.27 | 0.30	0.19 | 0.47	0.25 | 0.34	0.17 | 0.52	0.05 | 0.84
Ascending colon, r | P-	0.33 | 0.19	0.23 | 0.37	0.34 | 0.18	0.15 | 0.57	0.10 | 0.71

value					
Transverse colon, r | P-value	0.02 | 0.94	0.14 | 0.59	0.10 | 0.71	0.09 | 0.72	0.10 | 0.70
Descending colon, r | P-value	-0.09 | 0.73	0.08 | 0.75	0.15 | 0.56	0.07 | 0.80	-0.10 | 0.70
Rectosigmoid colon, r | P-value	0.18 | 0.50	0.52 | 0.94	0.16 | 0.54	0.13 | 0.61	0.12 | 0.65

Discussion

This study investigated whether correlations between subjective and objective measures of constipation were present, when investigated in a controlled experimental setting in which self-reported GI symptoms were categorized into relevant groups. No correlations between the measures could be demonstrated.

Our results are in line with previous studies. Thus, a study by Cowlam et al., found no association between symptom severity (overall PAC-SYM score) and total GI transit time in patients with chronic constipation (Cowlam et al., 2008). Additionally, another study found only a poor correlation of subjective constipation symptoms, assessed by the Cleveland Constipation Score and Rome Criteria III, and colonic transit time (Knudsen, Krogh, Østergaard, & Borghammer, 2017). The lack of correlations between these measurements likely reflects the multifaceted and very subjective experience of abnormal GI function.

We developed a new method to categorize GI symptoms assessed by questionnaires into relevant groups. This method has several advantages. Firstly, the procedure for selecting the symptoms included three requirements, which ensured that only the relevant symptoms were included i.e. the ones measurable by the objective measures and those experienced by ≥ 15 % of the participants. Secondly, as the symptoms were categorized based on their relation to each other (e.g. symptoms related to the act of defecation were placed in 'defecation difficulties') it was possible to analyse if any correlation between a specific group of related symptoms and the objective measures was present. Alternatively, the correlation between each of the objective measures and each single question of the questionnaires representing a symptom could have been investigated; however, this would have resulted in 400+ correlation analyses, thereby greatly increasing the risk of type I errors. Due to the many endpoints, any adjustment of the *P*-value would considerably decrease the chance of finding a true significant correlation.

As the method of categorizing symptoms into groups is new and not yet validated, results should be interpreted with caution. However, limitations related to the applied questionnaires and objective measures should also be recognized. The wordings and scales of the BFI, GSRS, and PAC-SYM vary, even though the questions address the same symptoms. This may potentially cause inter- and intra-individual variability, such as one participant might have understood one question differently than another participant (Olesen & Drewes, 2011). Physicians often define constipation as a reduction in stool frequency (typically as less than three defecations per week, as defined by the ROME IV criteria (Simren, Palsson, & Whitehead, 2017)) whilst patients typically think of constipation as a disorder combining multiple symptoms such as abdominal discomfort, straining, and the feeling of incomplete evacuation (Johanson & Kralstein, 2007). To give an example, in the BFI questionnaire, participants were asked to report their personal judgement on constipation severity; however, a clear definition of constipation was not provided, and thus the questionnaires

could be ambiguously perceived. Other limitations considers the actual study design, as we found that about 25% of all symptoms asked upon in the three questionnaires were rarely experienced by the participants, indicating that several of the questions might be irrelevant when assessing constipation. An explanation for this may also be the short duration of opioid treatment of merely 5 days. Even though this was enough to induce both objectively- and subjectively-measurable GI changes in healthy subjects, we expect that a longer treatment period and higher doses of oxycodone as applied in chronic pain patients would lead to more pronounced symptoms. Thus, a correlation between subjective and objective measures in chronic constipation induced by e.g. opioids cannot be excluded. The 3D-transit system and MRI colonography applied to measure transit time and colonic volume respectively are well-validated methods (Haase et al., 2014; Mark et al., 2017; M. Nilsson et al., 2015). However, another important limitation of this study was missing MRI data. Thus, six participants had not expelled the capsule on day 5, which is a clear indication of constipation. Consequently, the colonic volumes, along with the total GI transit times, are likely underestimated compared to the corresponding subjective measures, which could have contributed to the lack of correlations.

It can be argued that the patient's quality of life is more dependent on how the patient feels compared to any physiological aspect of the disease, suggesting that subjective measures are essential to capture the patient's perspective of GI function. A study by Bell et al. found that during opioid treatment approximately half of the patients had normal stool frequencies (considered an objective measure), whilst still experiencing symptoms such as straining, bloating, and the feeling of incomplete bowel evacuation (Bell et al., 2009). This indicates that subjective measures are vital, and that even simple objective measures such as stool frequency might be an inaccurate measure of GI function.

In summary, a new method for categorizing GI symptoms of opioid treatment was presented; however, this was not able to show any significant correlations between subjective and objective measures of GI function in a controlled study of constipation. Our results, along with previous literature, point to that subjective and objective measures are equally important in assessment of constipation, and a combination of the two are recommended in clinical assessments and future studies of constipation and other GI diseases.

Declarations of interest

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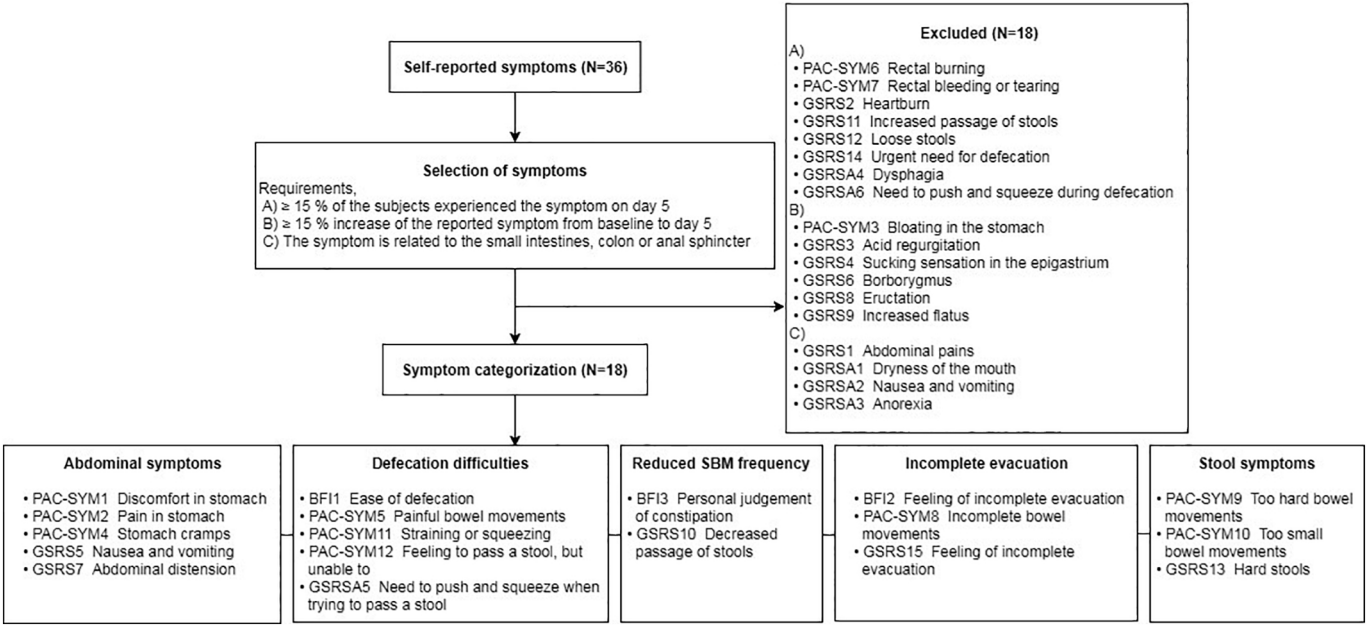
Self-reported symptoms (N=36)
Selection of symptoms
Requirements,
A) ≥ 15 % of the subjects experienced the symptom on day 5
B) ≥ 15 % increase of the reported symptom from baseline to day 5
C) The symptom is related to the small intestines, colon or anal sphincter
Excluded (N=18)
A)
• PAC-SYM6 Rectal burning
• PAC-SYM7 Rectal bleeding or tearing
• GSRS2 Heartburn
• GSRS11 Increased passage of stools
• GSRS12 Loose stools
• GSRS14 Urgent need for defecation
• GSRSA4 Dysphagia
• GSRSA6 Need to push and squeeze during defecation
B)
• PAC-SYM3 Bloating in the stomach
• GSRS3 Acid regurgitation
• GSRS4 Sucking sensation in the epigastrium
• GSRS6 Borborygmus
• GSRS8 Eructation
• GSRS9 Increased flatus
C)
• GSRS1 Abdominal pains
• GSRSA1 Dryness of the mouth
• GSRSA2 Nausea and vomiting
• GSRSA3 Anorexia
Symptom categorization (N=18)
Abdominal symptoms
• PAC-SYM1 Discomfort in stomach
• PAC-SYM2 Pain in stomach
• PAC-SYM4 Stomach cramps
• GSRS5 Nausea and vomiting
• GSRS7 Abdominal distension
Defecation difficulties
• BFI1 Ease of defecation
• PAC-SYM5 Painful bowel movements
• PAC-SYM11 Straining or squeezing
• PAC-SYM12 Feeling to pass a stool, but unable to
• GSRSA5 Need to push and squeeze when trying to pass a stool
Reduced SBM frequency
• BFI3 Personal judgement of constipation
• GSRS10 Decreased passage of stools
Incomplete evacuation
• BFI2 Feeling of incomplete evacuation
• PAC-SYM8 Incomplete bowel movements
• GSRS15 Feeling of incomplete evacuation
Stool symptoms
• PAC-SYM9 Too hard bowel movements
• PAC-SYM10 Too small bowel movements
• GSRS13 Hard stools

Figure 1

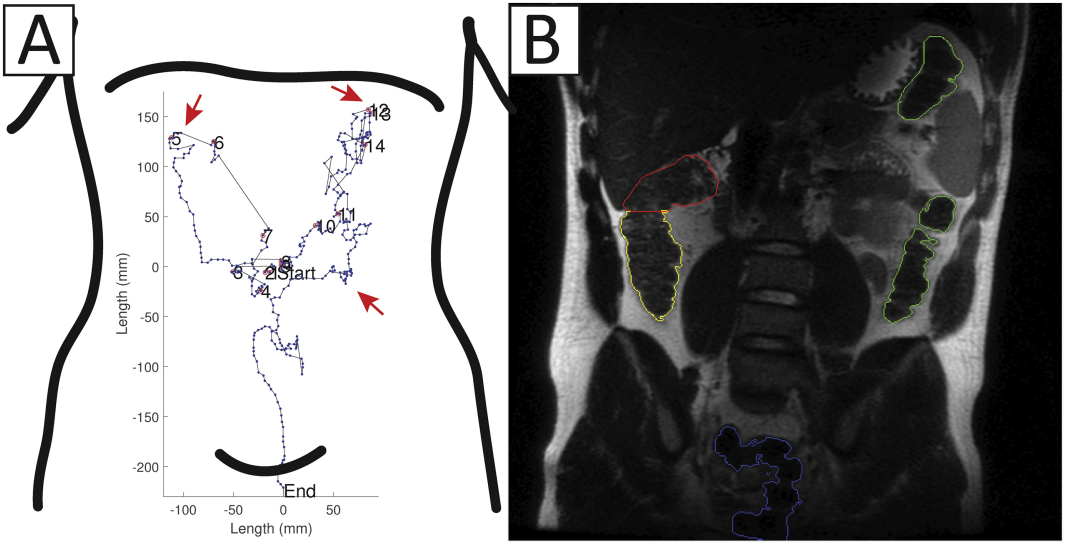

Figure 2